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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,302	01/10/2006	Kiyohiko Hatake	TOYA108.010APC	7332

20995 7590 02/28/2008

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
HUFF, SHEELA JITENDRA	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
02/28/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

Office Action Summary	Application No.	Applicant(s)	
	10/564,302	HATAKE ET AL.	
	Examiner	Art Unit	
	Sheela J. Huff	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-23,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-23 and 25-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/25/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment filed on 1/23/08 has been considered. Applicant's arguments are deemed to be persuasive-in-part.

Claims 14-23 and 25-26 are pending.

The rejection of claims 8-11, 20-22, 24 and 26 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for peptides consisting of aa residues 36-60 of SEQ ID NO. 1 and aa 36-61 of SEQ Id NO. 1, does not reasonably provide enablement for peptides having substitutions, deletions, additions or inversions of one or more amino acids residues in aa residues 36-60 of SEQ ID NO. 1 and aa 36-61 of SEQ Id NO. 1 is withdrawn in view of applicant's amendment.

The rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of applicant's amendments.

The rejection of claims 1-11 and 14-26 under 35 U.S.C. 102(a) as being anticipated by Sakurai et al Rinsho Ketsueki (8/30/04) vol. 45 p. 915 (submitted by applicant in IDS of 2/21/06) as evidenced by Yoo et al Jpn. J. Cancer Res. 88:184 (1997) is withdrawn in view of the translation of the priority document.

The rejection of claims 8-11 and 24 under 35 U.S.C. 102(b) as being anticipated by Nuijens et al US 6333311 or Tomita et al 5304633 is withdrawn in view of the cancellation of the claims.

The rejection of claims 1-7 under 35 U.S.C. 102(b) as being anticipated by JP 2000-229881 is withdrawn in view of the cancellation of the claims.

The rejection of claims 1-11 and 24 under 35 U.S.C. 102(b) as being anticipated by Yoo et al Jpn. J. Cancer Res. 88:184 (1997) as evidenced by page 12 of applicant's specification is withdrawn in view of the cancellation of the claims.

The rejection of claims 1-13 and 24 under 35 U.S.C. 102(b) as being anticipated by JP 08-073499 is withdrawn in view of the cancellation of the claims.

The rejection of claims 8, 10-11, 20, 22, 24, 26 under 35 U.S.C. 102(b) as being anticipated by WO 00/12542 is withdrawn in view of applicant's amendments **but will be re-instated if applicant amends the claims in response to the new matter rejection below.**

The rejection of claims 1-11, 14-17, 19-20, 22-26 under 35 U.S.C. 102(b) as being anticipated by Iigo et al Clinical And Experimental Metastasis vol. 17 p. 35 (1999) as evidenced by Yoo et al Jpn. J. Cancer Res. 88:184 (1997) is withdrawn in view of applicant's amendment.

Both rejections under 35 USC 103 are withdrawn amendments **but will be re-instated if applicant amends the claims in response to the new matter rejection below.**

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-22 and 26 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is essentially the same as that beginning on page 2 of the previous action. It is made because applicant changed "having" to "comprising" and both are open language. The rejection is re-worded below.

The claims are drawn to polypeptides comprising an amino acid sequence consisting of the amino acid sequence of SEQ ID no. 2 or 3. "Comprising" is open language therefore the claims read on peptide containing SEQ ID no. 2 or 3 with an unspecified length and composition of amino acids on either side of said sequences. While the amino acid sequence of SEQ ID no. 2 or 3 are adequately described in the specification as-filed, thereby providing an adequate basis for said sequences; there is insufficient written description as to the identity of a polypeptide comprising SEQ ID no. 2 or 3 that would still maintain the function of the polypeptide. Consequently, the specification does not provide an adequate written description of an polypeptides comprising SEQ ID no. 2 or 3.

The specification as filed does not provide adequate written description support for polypeptides comprising SEQ ID no. 2 or 3. Polypeptides having diverse functions

are encompassed by said polypeptides. Thus a broad genus having potentially highly diverse functions is encompassed by said polypeptides and conception cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. For example, Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., Abstract and Sequence-based approaches to function prediction, page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisans best guess as to the function of the structurally related protein (see in particular Abstract and Box 2). Adequate written description requires more than a mere statement that it is part of the invention. The sequence itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Therefore, only SEQ ID no. 2 or 3 meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed. (See page 1117.) The specification does not clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. (See Vas-Cath at page 1116.).

Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Response to applicant's arguments

Applicant argues that the claims have been amended to peptides which include SEQ ID NO. 2 or 3 which the Examiner said had written description. The Examiner said that SEQ ID 2 or 3 had sufficient written description not peptides that include SEQ ID NO. 2 or 3.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iigo et al Clinical And Experimental Metastasis vol. 17 p. 35 (1999) in view of Yoo et al Jpn. J. Cancer Res. 88:184 (1997), WO 00/12542, JP 2000-229881 and applicant's admission on page 2, lines 3-13 of the specification.

Iigo et al discloses the use of bovine lactoferrin, bovine lactoferrin hydrolyste (pepsin used for hydrolysis) and peptide lactoferricin (which is applicant's SEQ ID No. 2--see Yoo et al below) in combination in a medicament with anti-asialoGM1 antibody to inhibit tumor growth in lung and colon cancers in mice. Bovine lactoferrin hydrolyed with pepsin process the peptides or claim 8 as evidence by Yoo et al. Yoo et al shows that the pepsin generated peptide from bovine lactoferrin is FKCRRWQWRMKKLGAPSITCVRRAF (top of page 185-second column)(which is Seq ID No. 2 and aa residues 36-60 of SEQ Id NO. 1 of the instant invention). Iigo et al also

discloses the use of anti-asialoGM1 Ab, anti-CD4 mAb or anti-CD8 mAb with complement or complement alone also has an inhibitory effect (see Table 3).

Even though the reference is silent as to degradation rate of the lactoferrin hydrolysate, the average molecular weight, it is expected that the cow lactoferrin hydrosylate of the reference has the same properties as that of the reference because both use cow lactoferrin and the same enzyme for hydrolysis.

The only difference between the instant invention and the references is the treatment of breast cancer and the use of other anti-cancer antibodies such as anti-CD20, Anti-HER2 and Anti-17-1A and the use of the complement in combination with lactoferrin and anti-asialoGM1-ab.

WO 00/12542 discloses bovine lactoferrin peptide (LFB(17-41) in the abstract and this read on applicant's SEQ ID NO. 2 and aa 36-60 of SEQ ID No. 1) and its use in a medicament as an anti-tumor agent (see abstract). This reference also discloses the use of lactoferrin peptide with other active ingredients such as chemotherapeutics including antibodies (see p. 36). Also see page 26-27 and 34-36.

JP 2000-229881 discloses the use of cow lactoferrin digested with lactoferrin ([0063]) to treat cancer patients. The cancers include breast and colon (abstract, [0024]). This reference also discloses that a syngeristic effect can be expected by combining the use of digested cow lactoferrin with other anticancer agents)[0040]).

Applicant admits on page 2 of the specification that there are many known anti-cancer antibodies including Anti-CD20, anti-HER2 or Anti-17-1A.

In view of the fact, that there are many anti-cancer antibodies known in the art, including Anti-CD20, anti-HER2 or Anti-17-1A, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use the known anti-cancer antibodies in combination with the bovine lactoferrin, bovine lactoferrin hydrolyste (pepsin used for hydrolysis) and peptide lactoferricin of the primary reference with the expected benefit of cancer treatment. "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Furthermore, in view of the teachings in Iigo et al that the addition of complement also has an inhibitiory effect and in view of In re Kerkhoven it would have ben obvious to use complement with lactoferrin, the hydrolysate or lactoferrin peptide. It also would have been obvious to treat breast cancer because the JP document shows that lactoferrin and its hydrolysates can be used in such treatments and since it is known that Anit-HER2 is used in breast cancer treatment.

Response to applicant's arguments to the extent that the read on the instant rejection

Applicant argues that the teaching of complement in Iigo et al in Table shows that the best results were achieved with WBC alone and anti-CD4-mAb or anti-asialoGM1 and/or complement did not increase the survival rate of cancer cells. A close look at Table 3 shows that when WBC was used the number of surviving colonies was reduced

to 18.8 and that when complement was added, the number was still reduced, even in the present of antibody. Thus, the combination of lactoferrin, complement and antibody is obvious in view of the references. Claims 14-22 are compound claims and as such intended use carries no patentable weight when evaluating such claims.

Claim Rejections - 35 USC § 112

Claims 14-23 and 25-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

The claims now recite that the drug is composed of a lactoferrin hydrolystate, an antibody drug and a complement. The sections cited by applicant to provide support for “a complement” merely refer to “enhancing the action of complement” or “recovering the cytotoxic activity of complement” using the antibody drug/lactoferrin hydrolysate. Complement is not added as part of the drug. With respect to the Examples with state “addition of complement”, this complement as defined on page 29 of the specification is human serum AB obtained from Cosmobio. There is no objective evidence of record to show that human serum AB contains the complement proteins. Furthermore, even if human serum AB contains the complement proteins, applicant's claims states "a

complement"--meaning only one complement protein. The specification does not provide any support for the addition of a single complement protein.

Claims 14-23 and 25-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. In the claims, when using the terminology “a complement”, it is not clear if applicant is referring the complement proteins C1-C9 or some other protein that “complements” the antibody drug.

b. In claim 20 and 26 are unclear because they imply that the active ingredients are (a), (c). Re-writing the claims and putting the terminology after the colon in a wherein clause would clarify the claim.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Tuesday and Thursday from 5:30am to 1:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sheela J Huff/

Primary Examiner, Art Unit 1643